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09/826,212	04/05/2001	Ying-Fei Wei	1488.1280006	3523

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	8

DATE MAILED: 09/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/826,212	Applicant(s) WEI ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-116* is/are pending in the application.

4a) Of the above claim(s) *88-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-25,27,28,30,31,33-54,57-71,73-87 and 101-116* is/are rejected.

7)☒ Claim(s) *26,29,32,55,56,59,60,63,64 and 72* is/are objected to.

8)☒ Claim(s) *23-116* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-116 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 23-87 and 101-116 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the search and examination of Groups I through VII are related as drawn to polypeptides of SEQ ID NO: 2, and that even assuming that Groups I through VII represent distinct or independent subject matter, to search and examine the subject matter of the groups together would not be a serious burden on the Examiner, and that there is significant overlap between the polypeptides of Groups I through VII as evidenced by the identity in classification. Applicants' further point out that the Examiner has not addressed MPEP § 803.04, directed to nucleotide sequences, which holds that even when nucleotide sequences encoding different proteins are contained in an application, a reasonable number, normally ten, will be examined in a single application, and that the instant amino acid sequences constitute different fragments of the same protein, rather than different proteins as contemplated by MPEP § 803.04.

This is not found persuasive because contrary to Applicants' assertion that the instant amino acids constitute different fragments of the same protein and not different proteins, as written, the claims encompass a polypeptide comprising those small fragments of SEQ ID NO: 2, so that these fragments may be found in completely different proteins having different structures and functions. Additionally, thoroughly searching the seven groups would require seven separate polypeptide searches, as well as seven separate searches of the corresponding regions of

SEQ ID NO: 1, which would be fourteen separate searches, which would be a burden on the Office. As stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation a different field of search as defined in MPEP § 808.02." Further, due to the logarithmic increase in sequence database size, the PTO will no longer examine up to 10 sequences.

The requirement is still deemed proper and is therefore made FINAL.

Claims 88-100 are withdrawn as being drawn to a non-elected invention.

Claims 23-87 and 101-116 are currently under examination.

Priority

3. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/006,353. A statement reading "(now United States Patent No. 6,261,801)" should be included after "09/006,353 filed January 13, 1998" following the title of the invention or as the first sentence of the specification.

Information Disclosure Statement

4. The PTO-1449 filed XXX is present in the file. However, the references are not with the file and have not been found in the IDS storage facility. Therefore it is requested that Applicants submit a copy of the references for consideration with their response to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Claims 23-25, 27, 28, 30, 31, 33-44, 46-54, 57, 58, 61, 62, 65-71, 73-87, 101-102, 104, 105, 107, 108 and 110-116 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO:2, which is shown to have the following activities: binding TRAIL and blocking the ability of TRAIL to induce apoptosis. However, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that of SEQ ID NO:2 with the instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the

written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO:2. Given the unpredictability of altering amino acids in proteins and retaining activity, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The specification further sets forth that amino acids 27-123 are necessary for TRAIL binding activity, but the claims encompass polypeptides comprising only 30 or 50 contiguous amino acids of SEQ ID NO:2, which would therefore not retain TRAIL binding activity.

5.2 The enablement of claims 39-51 and 101-116 requires availability of the specific sequence claimed therein. This determination has been made because said cDNA clone is not fully disclosed nor have they been shown to be publicly known and freely available. Accordingly, it is deemed that a deposit of the cDNA clone should have been made in accordance with MPEP Chapter 2400 and 37 C.F.R. §§ 1.801-1.809. Applicant is advised that the Patent Office accepts Budapest approved deposits, as long as assurance is provided that the deposited material will be made irrevocably available with no restrictions upon issuance of patent. See MPEP Chapter 2400. An affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the deposit will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. It is acknowledged that a copy of a statement concerning the deposited cDNA clone was filed with the instant application, however the serial number of the application on the statement is that of the parent application, 09/006,353, and a new statement that has the serial number of the present application is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 73 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6.1 Claim 73 is indefinite because it is dependent upon claim 71, which encompasses an isolated polypeptide comprising 30 contiguous amino acids from amino acid 1 to 233 of SEQ ID

NO: 2, but claim 73 encompasses a polypeptide comprising amino acids 215-233 of SEQ ID NO: 2, which is less than 30 amino acids, and it is not clear if amino acids 204-214 are also to be included or not.

6.2 Claim 75 is indefinite because it encompasses a polypeptide which binds to an antibody with a specificity for a polypeptide consisting of amino acids **–26** to 233 of SEQ ID NO: 2, but it is dependent on claim 71, which encompasses a polypeptide comprising 30 contiguous amino acids from amino acid 1 to 233 of SEQ ID NO: 2, and it is not clear what limitation is encompassed by the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

7. Claims 71 and 74-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al., Database EST, Accession No. AA150541, May 19, 1997 (cited by Applicants), in view of Sibson et al. WO 94/01548 and Mosley et al. US Patent No. 5,783,672, filing date Sept.

12, 1994. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, which respect to the now claimed invention. The instant application claims benefit of provisional application 60/035,496, filed 01/14/1997, but this provisional does not meet the current utility requirements. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001. This prior application does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120. The instant application does receive benefit to priority of provisional application 60/054,885, filed 08/07/1997, because this provisional meets the utility requirements. Therefore, the effective priority date of the instant application is considered to be the filing date of provisional application 60/054,885, August 7, 1997.

These claims encompass an isolated polypeptide comprising 30 or 50 contiguous amino acids of SEQ ID NO: 2, wherein said polypeptide is produced by a recombinant host cell which may be eukaryotic, composition comprising the polypeptide and a carrier, wherein the polypeptide may also comprise a heterologous polypeptide which may be an Fc portion of an antibody.

Hillier et al. discloses a cDNA clone that is 100% identical to nucleotides 594-777 of the nucleic acid sequence of SEQ ID NO: 1, and which encodes amino acids 112-172 of the protein of SEQ ID NO: 2 (61 amino acids) (see attached sequence alignment). Hillier et al. does not teach the encoded protein, composition and carrier or fusion protein. Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector and host cell (eukaryotic) and to express the encoded protein, also as a fusion protein (see pages 8-13).

Mosley et al. teach composition comprising polypeptide and carrier, and fusion proteins comprising Fc domain (seen entire patent, and claims).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use Hillier et al.'s cDNA, expression vector, and host cell, to express and then isolate the encoded polypeptide or fusion polypeptide, as taught by Sibson et al., in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so in order to easily produce and analyze the encoded protein to determine its biological activity. It would also have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to put the polypeptide in a composition comprising a carrier and to make a fusion protein comprising an Fc domain, as taught by Mosley et al., since polypeptides in compositions can be used in assays to determine biological activity, for example, and fusion proteins comprising an Fc domain can be either easily purified or immobilized on agarose beads bearing Protein A and then used in assays to identify compounds which bind to the protein (see column 26, lines 11-32, for example). There would be a reasonable expectation of success of all of these methods, since they have been widely and successfully used in the field of molecular biology.

Conclusion

8.1 Claims 26, 29, 32, 55, 56, 59, 60, 63, 64 and 72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8.2 Claims 23-25, 27, 28, 30, 31, 33-54, 57-71, 73-87 and 101-116 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER